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| EXAMINER | |
|---|---|
| HINDENLANG, ALISON L | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/511,007 | PELLIKAAN ET AL. | |
| | Examiner | Art Unit | |
| | ALISON HINDENLANG | 1791 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *15-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Objections*

1. Claim 16 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The limitation "after the precipitated particles have grown to a volume weighted average diameter of at least 0.4 μm" (claim16) is broader than the limitation "after the precipitated particles have grown to a volume weighted average diameter of at least 1.0 μm" (claim 15).

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants' specification and arguments are directed to step d occurring after particles have grown to a volume weighted average particle diameter of at least 0.1 μm. The claim as amended reads "diameter of at least 1.0 μm". While the examiner finds this to be enabled by the disclosure of "at least 0.1 μm, preferably ... at least 0.4 μm" (specification page 6, lines 13-14), the magnitude of the difference between the disclosed and claimed ranges makes it unclear what the scope of the invention is.

4. Based on the specification and the arguments made in the remarks filed 11/14/2008, examiner understands the amended limitation of "at least 1.0 μm" to be a typo for 0.1 μm. Claims will be examined based on this understanding.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 15-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanna (US 6440337) (already of record).

7. With respect to claim 15, Hanna '337 teaches:

A process for the preparation of small particles through precipitation ("a method for forming particles of a substance", column 1, line 55), which process employs a fluid solution comprising a solvent and solute ("a solution or suspension of the substance in a vehicle", column 1, lines 58-59) to be precipitated and a supercritical or nearcritical antisolvent ("supercritical fluid", column 1, line 58), said solvent being soluble in or miscible with the antisolvent ("substantially soluble in the chosen supercritical fluid", column 3, lines 48-49) and said solute being substantially insoluble in the antisolvent, wherein the process comprises the successive steps of:

> a. feeding a stream of the fluid solution and a stream of the antisolvent into a mixing zone ("primary nozzle passages", column 6, line 57) where both streams are thoroughly mixed to achieve a condition of super saturation ("contact between a solution/suspension passing through the inner passage and a first supercritical fluid passing through a surrounding passage" column 6, lines 60-63);
>
> b. feeding the resulting mixture of the fluid solution and the antisolvent into a nucleation zone ("particle formation chamber", column 1, lines 56-57) allowing nucleation to commence; ("disperse the solution or suspension", column 1, lines 64)
>
> c. allowing the nuclei formed in the nucleation zone to grow ("extract the vehicle", column 1, line 65) to particles with a volume weighted average diameter of no more than

50 Am; ("median particle diameter 3276 nm", Table 1, Example 1)

d. collecting the particles ("collecting the particles", column 5, line 55) and separating them from the supercritical or nearcritical antisolvent ("recovering the solution", column 5, line 57) by depressurizing ("a separation vessel 9, where it is allowed to expand", column 9, lines 9-10, figure 1);

and wherein ... after completion of step a ... and prior to step d. additional antisolvent is admixed to the mixture of the fluid solution and the antisolvent. ("the outlets of the primary nozzle passages should be reasonably close to that of the secondary nozzle passage ... contact between a solution/suspension passing through the inner passage and a first supercritical fluid passing through a surrounding passage occurs inside the primary nozzle and before the two together contact the second supercritical fluid. Accordingly, a degree of dispersion and extraction can occur before further dispersion by the second supercritical fluid", column 6, lines 49-67).

Hanna '337 does not explicitly teach after "at least 1 second" or after particle growth to a weighted average diameter of at least 0.1 μm (see above).

Hanna '337 further teaches two fluid inlets which empty into a chamber simultaneously such that "dispersion of the solution or suspension, and extraction of the vehicle, to occur **substantially** simultaneously and **substantially** immediately on introduction of the fluids into the particle formation chamber" (column 3, lines 18-22 - emphasis added). Examiner understands "substantially simultaneously" and "substantially immediately" to include events which are delayed from each other by at least 1 second, though events separated by minutes would not be included.

Hanna '337 also teaches that "the actual distance and angle between them (nozzle passages) will depend, for instance, on the size, type, and shape of particles it is desired to form" (column 6, lines 52-55). Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to experiment with the timing of the step of adding additional antisolvent such that the particles grew to 0.1 μm (see above) before hand if so desired. It has been ruled that discovering optimum or workable

ranges involves only routine skill in the art. *See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235.*

8. With respect to claims 16 and 17, Hanna '337 does not explicitly teach "wherein the additional antisolvent is admixed after the precipitated particles have grown to a volume weighted average diameter of at least 0.4 μm" or "wherein the antisolvent is admixed at least 3 seconds after completion of step a".

The further teachings of Hanna '337 regarding "substantially simultaneously" are understood to include events separated by at least 3 seconds while the teachings regarding particle size and shape being dependent upon apparatus design are considered sufficient motivation for experimentation. Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to experiment with the timing of the step of adding additional antisolvent such that the particles grew to 0.4 μm before hand if so desired. It has been ruled that discovering optimum or workable ranges involves only routine skill in the art. *See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235.*

9. With respect to claim 18, Hanna '337 further teaches:

> wherein the ratio of the solution flow rate to antisolvent flow rate in step a. is between 5:1 and 1:10 ("the ratio of the solution/suspension flow rate to each supercritical fluid flow rate will be between 0.001 and 0.2", column 3, lines 1-3)

10. With respect to claim 19, Hanna '337 discloses the claimed invention except for "wherein the collected particles, when reaching the end of the nucleation zone or immediately prior to the admixture of additional antisolvent, contain at least 1 wt % solvent". It would have been obvious to one having ordinary skill in the art at the time of

the invention to maintain fluid flow rates such that some of the solvent vehicle remained present after the initial addition of antisolvent for the purpose of controlling particle size since Hanna '337 discloses that "the size of the fluid elements formed on dispersion, will depend on the relative flow rates of the fluids" (column 6, lines 46-48) and it has been held that where the general condition of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. One would have been motivated to maintain fluid flow rates such that some of the solvent vehicle remained present after the initial addition of antisolvent for the purpose of controlling particle size. *See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235.*

11. With respect to claim 20, Hanna '337 discloses the claimed invention except for "wherein the additional antisolvent is admixed in an amount effective to reduce the solvent content of the collected particles to less than 1 wt %". It would have been obvious to one having ordinary skill in the art at the time of the invention to control the fluid flow rates such that the amount of solvent present in the collected particles is low because this aids in particle formation control since Hanna '337 discloses that "the vehicle will represent no more than around 5% mole fraction of the supercritical fluids" (column 5, lines 23-24) which "allows improved control over particle characteristics and substantially eliminates the risk of residual vehicle in the particulate product" (column 5, lines 30-32) and it has been held that where the general condition of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. One would have been motivated to control the fluid flow rates such that the amount of solvent present in the collected particles is low because this

aids in particle formation control. *See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235.*

12. With respect to claim 21, Hanna '337 further teaches:

wherein less than 25% of the nuclei ("a degree of dispersion and extraction", column 6, line 65) formed in the process are formed in the mixing zone ("before further dispersion by the second supercritical fluid", column 6, lines 66-67)

13. With respect to claim 22, Hanna '337 further teaches:

wherein the residence time within the mixing zone is less than 15 seconds. ("the first and second supercritical fluids will usually, although not necessarily, meet at or very close to the point of particle formation, ie, the point at which they contact the solution or suspension", column 3, lines 35-38)

14. With respect to claim 23, Hanna '337 discloses the claimed invention except for "wherein the mixing energy applied in the mixing zone exceeds 1 J/kg". It would have been obvious to one having ordinary skill in the art at the time of the invention to apply significant amounts of energy to the mix zone for the purpose of providing a high degree of dispersion in order to control particle uniformity since Hanna '337 discloses that "the solution/suspension can be subjected to a very high degree of dispersion due to the high overall supercritical fluid velocity (ie, high overall kinetic energy)" (column 2, lines 33-35) which "can provide a high degree of uniformity in the particles formed" (column 2, lines 37-38) and it has been held that where the general condition of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. One would have been motivated to apply significant amounts of energy to the mix zone for the purpose of providing a high degree of dispersion in order to control particle uniformity. *See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235.*

15. With respect to claim 24, Hanna '337 discloses the claimed invention except for "wherein the residence time within the nucleation and growth zone is at least 3 seconds". It would have been obvious to one having ordinary skill in the art at the time of the invention to modify the length of the growth zone and the residence time therein in order to control particle size. since Hanna '337 discloses that "the size and shape of the intermediate chamber may be used in part to determine the characteristics of the particles formed" (column 7, lines 49-51) and it has been held that where the general condition of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. One would have been motivated to modify the length of the growth zone and the residence time therein in order to control particle size. *See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235.*

16. With respect to claim 25, Hanna '337 further teaches:

wherein the solution comprises between 0.0001 and 30 wt.% of the solute. ("a 0.625% w/v solution of nicotinic acid in absolute ethanol", column 13, lines 10-11, example 1)

17. With respect to claim 26, Hanna '337 further teaches:

wherein the antisolvent is a supercritical fluid ("a fluid substantially at or above its critical pressure (Pc) and critical temperature(Tc) simultaneously", column 3, lines 40-42).

18. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hanna (US 6440337) as applied to claim 15 above, and further in view of Hanna (US 6576262) (already of record). Hanna '337 remains as applied above. Hanna further teaches that the use of two supercritical fluid flows results in "a high degree of uniformity in the particles formed" (column 2, lines 37-38). Hanna '337 does not teach:

wherein the particles obtained from step c. have a particle size distribution with a standard deviation of less than 50% of the volume weighted average particle size.

In the same field of endeavor, the production of particles via precipitation with supercritical fluids, Hanna '262 teaches a process using two supercritical fluids where the product has a mean size of 14.13 μm and a standard deviation of 1.611 (column 14, example 2, table 4) for the benefit of producing uniform solute particles with high purity. It would have been obvious to one of ordinary skill in the art at the time of the experiment to modify the process taught by Hanna '337 using conditions taught by Hanna '262 for the benefit of producing uniform solute particles with high purity.

19. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hanna (US 6440337) as applied to claim 15 above, and further in view of Avontuur (US 6830714) (already of record). Hanna '337 remains as applied above. Hanna '337 does not teach:

wherein at least 10 wt.% of the solute present in the stream of the fluid solution of step a. is recovered in the particles obtained in step d.

In the same field of endeavor, the production of particles via precipitation with supercritical fluids, Avontuur '714 teaches, "the proportion of nabumetone was consistent between 78.9 – 80.5 % w/w over a number of runs of the process" (example 3, column 15, lines 26-27) for the purpose of isolating and recovering the starting solute in small, fine particles. It would have been obvious to one of ordinary skill in the art at the time of the experiment to modify the process taught by Hanna '337 using conditions taught by Avontuur '714 for the purpose of isolating and recovering the starting solute in small, fine particles.

***Response to Arguments***

20. Applicant's arguments filed 11/14/2008 have been fully considered but they are not persuasive.

21. Regarding the 102(e) rejection of claims 15, 17-18, 21-22, and 25-26 of the first action, Applicant argues that Hanna '337 does not teach all the limitations of claim 15 specifically the 1 second and 0.1 μm limitations added by amendment. The rejection has been changed to a single reference 103 rejection in order to overcome these new limitations.

22. As applied in the rejection of this action, Hanna '337 teaches two fluid inlets which empty into a chamber simultaneously such that "dispersion of the solution or suspension, and extraction of the vehicle, to occur **substantially** simultaneously and **substantially** immediately on introduction of the fluids into the particle formation chamber, by the action of **either or both** of the two supercritical fluids" (column 3, lines 18-23 - emphasis added). Examiner understands "substantially simultaneously" and "substantially immediately" to include events which are delayed from each other by at least 1 or 3 seconds. Further more Examiner understands the statement that dispersion and extraction occurs by "the action of either or both" of the supercritical fluids to mean that Hanna '337 discloses an embodiment in which one supercritical fluid acts on the solution/suspension before the other.

23. Regarding the single reference 103 rejections of claim 16, 19-20, and 23-24 of the first action, Applicant argues that there is no motivation to alter the teachings of

Hanna '337. First because the second supercritical fluid taught by Hanna '337 is used for a different purpose than that of the instant invention and second because Hanna '337 teaches away from the 1 second and 0.1 μm limitations. Applicant further asserts that any alterations to the teachings of Hanna '337 are improper hindsight.

24. With regard to the first argument examiner wishes to point out the concept of intended use holds for method steps as well as structural elements and that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. Hanna '337 discloses every step of the method claimed. The discovery that a claimed step has a result unknown to the prior art does not distinguish the method from that of the prior art. Furthermore Examiner wishes to point out that Hanna '337 discloses the use of the second supercritical fluid to "provide a high degree of uniformity in the particles formed" (column 2, lines 37-38) which is the reason Applicant gives.

25. Examiner does not find Hanna '337 to teach away from the instantly claimed limitations. While Hanna '337 focuses on embodiments in which the two supercritical fluids contact the solution/suspension "substantially simultaneously", Hanna '337 does not teach that sequential or chronologically separated contact would negate the disclosed invention. In fact Hanna '337 repeatedly discloses alternative embodiments:

a. "dispersion of the solution or suspension, and extraction of the vehicle, to occur substantially simultaneously and substantially immediately on introduction

of the fluids into the particle formation chamber, by the action of either or both of the two supercritical fluids" (column 3, lines 18-23)

b. "The first and second supercritical fluids will usually, although not necessarily, meet at or very close to the point of particle formation, ie, the point at which they contact the solution or suspension" (column 3, lines 35-37)

c. "contact between a solution/suspension passing through the inner passage and a first supercritical fluid passing through a surrounding passage occurs inside the primary nozzle and before the two together contact the second supercritical fluid" (column 6, lines 60-65)

and teaches that particle size and shape is dependent not only on the distance between the supercritical fluid contact points but also on the choice of supercritical fluid, the fluid flow rates and manufacturing constraints such as nozzle and chamber geometry.

26. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Since Examiner uses only teachings disclosed by Hanna '337 to motivate the conclusion of obviousness the reasoning is not improper.

27. Regarding the 103 rejection of claim 27 over Hanna '337 in view of Hanna '262, Applicant argues that Hanna '337 teaches away from the 1 second and 0.1 μm limitations and that Hanna '262 does not satisfy this deficiency thus negating any expectation of success in the combination.

28. Examiners' reasoning as to why Hanna '337 does not teach away from the instant limitations has been clearly stated above as have Examiners' reasons for concluding that Hanna '337 motivates one of ordinary skill in the art to experiment with and optimize multiple factors for the purpose of producing particles with desired size and uniformity. As Applicant does not argue the teachings of Hanna '262 outside of arguing motivation to combine, applicant's arguments are not found to be persuasive.

29. Regarding the 103 rejection of claim 28 over Hanna '337 in view of Avontuur '714, Applicant argues that Hanna '337 teaches away from the 1 second and 0.1 μm limitations and that Hanna '262 does not satisfy this deficiency thus negating any expectation of success in the combination.

30. Examiners' reasoning as to why Hanna '337 does not teach away from the instant limitations has been clearly stated above as have Examiners' reasons for concluding that Hanna '337 motivates one of ordinary skill in the art to experiment with and optimize multiple factors for the purpose of producing particles with desired size and uniformity. As Applicant does not argue the use of the teachings of Avontuur '714 other than when arguing motivation to combine, applicants' arguments are not found to

be persuasive.

31. Finally, the instant specification does not show that the particles achieved by the instant process would differ significantly from those produced by the process of Hanna '337. It has been ruled that given substantially similar results, steps taken concurrently or simultaneously are equivalent. *See New Wrinkle vs Marzall (93 USPQ 92) or New Wrinkle vs. Watson (94 USPQ 436).*

***Conclusion***

32. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALISON HINDENLANG whose telephone number is (571) 270-7001. The examiner can normally be reached on Monday to Thursday 7:30 - 5 pm; Every other Friday 7:30 - 4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Philip Tucker can be reached on 571-272-1095. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ALH

/Philip C Tucker/
Supervisory Patent Examiner, Art Unit 1791